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Group Art Unit: 1638

REMARKS

Claim Rejections – 35 USC §112, Second Paragraph

Claims 1-5, 7-8, 10, 13-14, 17-18, 20-21, 23, 26-27, 30, 32-33, 35, 38-39, 42-47, 49, 53, and 57 have been rejected by the Examiner under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner states that in Claim 1, the metes and bounds of "capable" are not defined. The Applicants have amended Claim 1 so as to obviate the rejection. Applicants note that the term "capable" also appeared in Claims 17 and 43, and those claims have been amended accordingly.

The Examiner states that in Claim 1, the metes and bounds of "regulated expression" are not defined. The Applicants have amended Claim 1 so as to obviate the rejection.

The Examiner states that in Claim 1, the metes and bounds of "cytokinin modulating gene" are not defined. All subsequent recitations of "cytokinin modulating gene" have also been rejected. The Applicants have amended Claim 1, and amended (Claims 30, 43, 49, 53) or canceled (Claims 5, 18, and 57) other claims in which the offending phrase appears, so as to obviate the rejection.

The Examiner states that in Claim 1, the term "gene" is indefinite. The Applicants have amended Claim 1, and have amended (Claims 13, 14, 26, 27, 38, and 39), withdrawn (Claims 50, 51, 54, 55, and 58) or canceled (Claims 5 and 18) other claims in which the term "gene" appears, so as to obviate the rejection. The term "gene expression" does remain in Claim 30, and Applicants submit that such term is understood by those of skill in the art.

The Examiner states that the metes and bounds of "preferential" have not been defined in Claim 1 and asks how one would measure or assess if a spatial or temporal expression pattern is "preferential." All subsequent recitations of "preferential" have also been rejected. The Applicants have amended Claim 1 so as to obviate the rejection. Claim 1 now states that expression is driven by a promoter which is "tissue-preferred, tissue-specific, or temporally-regulated." Applicants direct the Examiner's attention to pages 14,

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28, and 29 of the specification, where ample support for these terms is provided. In addition, Example 3 (pages 52-53) and Figure 1 provide an example of how one would assess preferential expression. In Figure 1A, embryo cytokinin levels are increased from 2- to 8-fold (i.e., 200% to 800%) over controls. In Figure 1B, endosperm cytokinin levels are increased only 10% to 30%. This indicates preferential expression in the embryo.

The Examiner states that in Claim 1, the metes and bounds of "sufficient" have not been defined. The Applicants have amended Claim 1 so as to obviate the rejection.

The Examiner has rejected Claim 1 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. The Applicants have amended Claim 1 to include the omitted step and thank the Examiner for pointing out the need to do so.

The Examiner states that in Claims 5 and 7, "seed" should be replaced with "seeds." Claim 5 has been canceled; Claims 7 and 20 have been amended to obviate the rejection; Claims 17, 30, and 32 have been amended as suggested.

The Examiner states that in Claim 5, the word "operatively" should be replaced with "operably." Claim 5 has been canceled; Claim 30 has been amended to replace the word "operatively" with "operably."

The Examiner states that in Claims 5, 18, and 30 it is unclear if the "promoter" or the "plant seed" is linked to a gene. Claims 5 and 18 have been canceled; Claim 30 has been amended to clarify that the promoter is operably linked to the isolated polynucleotide of interest, as have Claims 1, 17, and 43.

The Examiner has rejected Claim 8 for being indefinite as to the metes and bounds of "embryo preferred expression." Applicants respectfully direct the Examiner's attention to pages 14, 28, and 29 of the specification, where ample support for this term is provided.

The Examiner has rejected Claim 10 for being indefinite as to the metes and bounds of "endosperm-preferred expression." Applicants respectfully direct the Examiner's attention to pages 14, 28, and 29 of the specification, where ample support for this term is provided.

The Examiner has rejected Claim 13 for use of the term "modulating." All subsequent recitations of "modulating" have also been rejected. The Applicants have amended or canceled claims so as to eliminate use of the term "modulating."

The Examiner has rejected Claim 13 for being indefinite as to the metes and bounds of "cytokinin biosynthetic enzyme" and asks how one would measure or assess whether an

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enzyme is considered to be a "cytokinin biosynthetic enzyme." The Applicants respectfully assert that the term is unambiguous to one of skill in the art. While it could conceivably be postulated that every physiological process in an organism is in some way related to biosynthesis of a single, specific product, such an extrapolation would render meaningless much of the vocabulary of physiology and would be unreasonable to one of skill in the art. In support of this position, and to further define "cytokinin biosynthetic enzyme," the Applicants refer the Examiner to Biochemistry & Molecular Biology of Plants (Buchanan, Gruissem & Jones, eds., American Society of Plant Physiologists, Rockville, MD, 2000), particularly pages 874-877, which represents the state of knowledge of cytokinin biosynthesis at the time the application was filed. Applicants submit that the enzymes therein identified as involved in cytokinin biosynthesis comprise "cytokinin biosynthetic enzymes" of the invention.

The Examiner has pointed out that "transferase" was misspelled in Claim 1-1. Applicants thank the Examiner for pointing out the error and have made the correction.

The Examiner states that in Claim 17, the term "modulation" is unclear. Applicants have amended or canceled claims in order to obviate the rejection.

The word "molecule" has been inserted after "DNA" in Claim 30, as suggested by the Examiner.

The Examiner has rejected Claim 43 for use of the term "yield stability." The Applicants respectfully respond that "yield stability" relates to consistent performance of a given genotype across environments and is a term that would be known to one of skill in the art. A search of Biological Abstracts on "yield stability" yielded 495 hits and indicates that the term was in use in scientific publications as early as 1967. A definition in the description is therefore not required.

The Examiner has rejected Claim 43 for indefiniteness as to the metes and bounds of "preferentially." Claim 43 has been amended to remove the word "preferentially"; however, claims 44-47 refer to "preferential" expression. Applicants direct the Examiner's attention to pages 14, 23, and 29 of the specification, where ample support for this term is provided. In addition, Example 3 (pages 52-53) and Figure 1 provide an example of how one would assess preferential expression. In Figure 1A, embryo cytokinin levels are increased from 2- to 8-fold (i.e., 200% to 800%) over controls. In Figure 1B, endosperm cytokinin levels are increased only 10% to 30%. This indicates preferential expression in the embryo.

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The Examiner has rejected Claim 43 for indefiniteness as to the term "lag phase." The Applicants respectfully respond that "lag phase" is a term known to one of skill in the art. For example, see Cheikh and Jones, Plant Physiology 106:45-51, 1994; the first line of the article states: "The first 10 to 12 DAP (the lag phase) is a critical period during kernel development in maize." (DAP refers to days after pollination.) Thus, a definition in the specification is not required.

The Examiner has rejected Claim 43 as being incomplete for omitting essential steps. Claim 43 has been appropriately amended to overcome the rejection.

The Applicants respectfully ask that all rejections under 35 USC 112, second paragraph, be withdrawn.

Claim Rejections – 35 USC §112, First Paragraph, Written Description

Claims 1-5, 7-8, 10, 13, 17-18, 20-21, 23, 26, 30, 32-33, 35, 38, 42-47, 49, 53 and 57 have been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner states that "the specification fails to describe adequate representative numbers of cytokinin modulating genes, or cytokinin biosynthetic enzymes, which encompass any gene which directly or indirectly, in any pathway, affect the expression of cytokinin or affect the level of already expressed cytokinin by any method (binding, antagonists, protagonists, competitive binding, antibodies, etc)." The Examiner cites the Written Description Examination Guidelines published in the Federal Register, Vol. 66, No. 4, Friday, January 5, 2001 (hereinafter "Guidelines").

The Applicants traverse the rejection and state that an adequate number of cytokinin modulating genes are described. The sequence listing provides both *ipt* and cytokinin oxidase sequences. Other cytokinin modulating genes are referred to generally at page 3, lines 8-17, including genes encoding enzymes involved in conjugation, hydrolysis, reduction, and oxidation, and in particular those enzymes "associated with rate-limiting steps." This description would reasonably convey to the skilled artisan what is encompassed by the invention. According to the Guidelines, "a single species may, in some instances, provide

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an adequate written description of a generic claim..." (at p. 1102, comment 16). Further, "what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d at 1384, 231 USPQ at 94.

The Examiner further states that "[t]he specification also does not describe an end2 promoter or its expression profile. Applicant only reference provisional applications and a non-provisional application (page 29, top paragraph) but they fail to disclose within the present application the necessary information needed by one skilled in the art to identify an end2 promoter. "

The Applicants traverse the rejection and respond that the referenced U.S. patent applications, 60/098,230 and 09/383,543, adequately describe the end2 promoter. There is no need for "the present application" to disclose the necessary information needed by one skilled in the art to identify an end2 promoter if such information is provided in a proper reference.

"The test for determining compliance with the written description requirement is whether the disclosure as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." *In re Kaslow*, 707 F.2d 1366, 217 USPQ 1089 (Fed. Cir. 1983)

Furthermore, the test is not whether the public was in possession of the invention at the time the application was filed, but whether the applicant was in possession. The fact that the Applicants were able to provide the application number for the provisional application on the end2 promoter is itself evidence that Applicants were in possession of the end2 promoter used in the invention. The January 21, 2003, amendment in the present case, inserting (at pages 28-29 of the specification) the application number (09/383,543) for the utility patent which issued on March 4, 2003, and which claims the benefit of the earlier provisional application 60/098,230, is further evidence that the Applicants met the written description requirements under 35 USC 112, first paragraph, with respect to the end2 promoter.

As the Federal Circuit has held (*Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000)), "The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she]

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invented what is claimed.' Thus, Section 112 Paragraph 1, ensures that, as of the filing date, the inventor conveyed with reasonable clarity to *those of skill in the art* that he was in possession of the subject matter of the claims." (citations omitted, emphasis added). (from Guidelines, p. 1103)

The Applicants also note the reminder in the Guidelines (p. 1100) that "there is a 'strong presumption' that an adequate written description of the claimed invention is present when the application is filed, consistent with *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)." Thus, the Applicants respectfully ask that the rejections as to written description be withdrawn.

Claim Rejections – 35 USC §112, First Paragraph, Enablement

The Examiner has stated that the specification is enabling for a maize plant transformed with an isopentenyl-transferase-encoding polynucleotide (ipt) to produce seeds with increased zeatin levels, increased seed set compared to plants transformed with other genes (page 56, Table 2) and seeds that exhibit vivipary.

The Examiner has rejected Claims 1, 4, 7-8, 10, 13, 17-18, 20-21, 23, 26, 30, 32-33, 35, 38, 42-47, 49, 53, and 57 for lack of enablement for claims drawn to

- (1) a method of producing a transgenic plant that regulates cytokinin levels in developing seeds, comprising transforming a plant with a cytokinin modulating gene operably linked to an end2 promoter, wherein the cytokinin modulating gene encodes a cytokinin biosynthetic enzyme;
- (2) a transgenic plant comprising a construct that affects the cytokinin levels in seeds, wherein the construct comprises a cytokinin modulating gene operably linked to an end2 promoter and wherein the cytokinin modulating gene encodes a cytokinin biosynthetic enzyme; or
- (3) an isolated recombinant DNA molecule and a method for improving stress tolerance and yield comprising a construct comprising a cytokinin modulating gene operably linked to an end2 promoter wherein the cytokinin modulating gene encodes a cytokinin biosynthetic enzyme.

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In addition, the Examiner states that enablement is not provided for promoters that direct embryo- or endosperm-preferred expression or promoters that preferentially express from about 14 to 25 days after pollination (DAP), 4 to 21 DAP, 4 to 12 DAP or 8 to 12 DAP.

The Examiner first rejects claims based on the breadth of the term "modulating." Amended claims submitted herewith no longer use the term "modulating"; claim breadth has been narrowed to encompass cytokinin biosynthetic enzymes and cytokinin catabolic enzymes. Thus, this rejection has been obviated.

The Examiner goes on to state that there are multiple cytokinin biosynthetic pathways in plants and that not all cytokinin biosynthetic enzymes are known. The Applicants refer the Examiner to the specification, particularly the bottom of page 2 through the first full paragraph of page 3, which provides support for known cytokinin biosynthetic enzymes. To further expedite prosecution, the Applicants have provided claims 14, 27, 39, 53, and 60-63, in which the isolated polynucleotide is limited to one which encodes isopentenyl transferase.

The Examiner cites Kusaba et al. (Plant Physiology 116(2):471-476) as teaching that unpredictable results may be obtained when cytokinin activity is modulated. The Applicants respectfully point out that the cited research reported transformation with a construct comprising a constitutive promoter. In contrast, the present invention specifically provides that the isolated polynucleotide encoding a cytokinin biosynthetic enzyme be operably linked to a tissue-preferred, tissue-specific, or temporally-regulated promoter. See, for example, the spec at page 4, lines 14-21 and lines 31-33; and page 6, lines 19-26 and 31-34. Thus the invention is distinct from Kusaba et al., in that spatially- or temporally-limited expression of the isolated polynucleotide affecting cytokinin levels is a fundamental component of the present invention; increasing the predictability of results.

The Examiner states that Applicants have not exemplified an end2 promoter. In response, Applicants direct the Examiner's attention to page 29, lines 12-13, of the specification, and to the amendment filed January 17, 2003, which provide the serial numbers for patent applications disclosing the end2 promoter.

The Examiner also states that Applicants have not taught or provided guidance as to embryo-preferred or endosperm-preferred promoters. In response, Applicants direct the Examiner's attention to the specification, pages 28 and 29, which provides numerous examples of appropriate promoters.

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The Examiner further states that using a promoter isolated from one species of plant would produce unpredictable results when said promoter is used to specify expression of a gene in another species of plant, citing the abstract of Oommenn et al. (Plant Cell 6:1789-1803, 1994). In response, the Applicants first point out that on page 1800 of the cited reference, the authors state that the recipient species, tobacco, does not possess the isoflavonoid branch of phenylpropanoid biosynthesis from which the alfalfa IFR promoter was derived. A similar situation does not exist in the present application. Second, it would be within the realm of reasonable experimentation for one of skill in the art to test a promoter for efficacy in the chosen species.

As provided in *Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991), "The enablement requirement is met if the description enables any mode of making and using the claimed invention."

The Applicants respectfully ask that all rejections as to enablement be withdrawn.

Claim Rejections – 35 USC §102

Claims 1-2, 4-5, 13-14, 17-18, 26-27, 30, 38-39, 42-43, 49, 53, and 57 have been rejected as being anticipated by Houck et al. (U.S. Patent No. 5,177,307).

Houck et al. disclose and claim an expression cassette comprising the 2AII, Z130, or Z70 promoter, as well as tomato plant cells, tomato fruits, and methods of modifying tomato fruits, all comprising said expression cassette.

The Applicants respectfully ask that the rejections as to anticipation be withdrawn. "For a prior art reference to anticipate in terms of 35 U.S.C. 102, every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 910 F.2d 833, 15 USPQ2d 1566 (Fed. Cir. 1990). The present application is distinct from the Houck et al. patent as to several elements and thus is not anticipated.

For example, Houck et al. is directed to cytokinin modification so as to increase fruit weight and/or alter the rate of fruit ripening. In contrast, the present application provides utilities of improved seed size, decreased tip kernel abortion and increased seed set during unfavorable environmental conditions (see specification, bottom of p. 4).

Second, the tomato is the species of choice in the Houck application. A long list of other "fruit-bearing plants" is provided (paragraph bridging columns 8 and 9), and the patent

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states, "As a host cell, cells from any of a number of fruit bearing plants may be employed in which the plant parts of interest are derived from the ovary wall." (emphasis added) In contrast, the present application provides examples using *Zea mays*, not considered to be a "fruit bearing plant." In fact, the list in the '307 patent includes no monocots.

Further, the present application claims (Claims 43 and 63) a method to result in improved stress tolerance and yield stability, which is supported by the specification at page 6. While the Examiner states (p. 14 of Office Action) that improved stress tolerance and yield stability would be "an inherent feature" of seeds with modulated cytokinin levels, the Applicants find no such claim or description in the '307 patent. The Federal Circuit has ruled that "[A] retrospective view of inherency is not a substitute for some teaching or suggestion which supports the selection and use of the various elements in the particular claimed combination." In re Newell, 891 F.2d 899, 13 USPQ2d 1248 (Fed. Cir. 1989), *cert. denied*, 493 U.S. 814 (1989). This position was further confirmed by the Court's statement that, "The mere fact that a certain thing *may result* from a given set of circumstances is insufficient to prove anticipation." Electro Medical Systems, S.A. v. Cooper Life Sciences, Inc., 34 F.3d 1048, 32 USPQ2d 1017 (Fed. Cir. 1994)

In view of the lack of identity between U.S. Patent 5,177,307 and the present application, there is no anticipation, and Applicants respectfully ask that the rejections as to 35 USC 102 be withdrawn.

Claim Rejections – 35 USC §103

Claims 1-5, 8, 10, 13-14, 17-18, 21, 23, 26-27, 30, 33, 35, 38-39, 42-47, 49, 53, and 57 have been rejected as being unpatentable over Houck et al. (U.S. 5,177,307) in view of Tomes et al. (U.S. 5,877,400). The Examiner states that, "It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to transform a plant with an *ipt* gene as taught by Houck et al. using the embryo and endosperm expressing promoters of Tomes, so as to express the *ipt* gene in developing seeds with a reasonable expectation of success."

The Applicants respectfully traverse. A finding of obviousness must be supported by some suggestion, motivation, or teaching in the prior art that would have led a person of ordinary skill in the art to select the references and combine them in the way that would

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produce the claimed invention. Further, as provided in *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992), "That knowledge can not come from the applicant's invention itself." Also, "The fact that a prior art device could be modified so as to produce the claimed device is not a basis for an obviousness rejection unless the prior art suggested the desirability of such a modification." *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) (emphasis added)

U.S. Patent 5,177,307 is directed to cytokinin modification so as to increase fruit weight and/or alter the rate of fruit ripening. The tomato is the species of choice in the application, although a long list of other "fruit-bearing plants" is provided (paragraph bridging columns 8 and 9). Specifically, the patent states, "As a host cell, cells from any of a number of fruit bearing plants may be employed in which the plant parts of interest are derived from the ovary wall." No monoxot species are included in this list.

"An analysis of obviousness of a claimed combination must include consideration of the results achieved by that combination." (emphasis added) *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 16 USPQ2d 1923 (Fed. Cir. 1990) In this respect, it is important to note that U.S. Patent 5,877,400 is directed to modification of fruit development, in particular altering the timing of development so as to *minimize seed production*. ("The method also results in a fruit that has diminished or very little seed." [400 abstract]) A combination of the '307 and '400 patents would in fact teach away from the current invention, which is directed toward *maximum* seed growth.

Thus, one skilled in the art of the present invention would not likely be motivated to combine the disclosures of 5,877,400 (providing promoters to be used in minimizing seed production) and 5,177,307 (providing a means to modify fruit ripening) to create constructs, methods, and plants directed toward increased grain (i.e. seed, not fruit) yield. Further, the present application is directed toward plant performance in an unfavorable environment, a factor which is not suggested in either patent.

Hindsight reconstruction of the pending invention is not permissible and is best avoided by a specific showing of the teaching or motivation to combine prior art references. See, for example, *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998), 48 USPQ 2d 1225, 1232 (Fed. Cir. 1998), which describes a 'teaching or suggestion or motivation [to combine]' as an 'essential evidentiary component of an obviousness holding.' Also see *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227

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USPQ 657, 667 (Fed. Cir. 1985), in which the district court's conclusion of obviousness was found to be in error because it 'did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination'.

The Examiner having provided no prior art containing a teaching or suggestion to combine the cited references, and the results to be achieved by the combination of the cited references being contradictory to those of the instant application, the Applicants respectfully ask that the rejections as to obviousness be withdrawn.

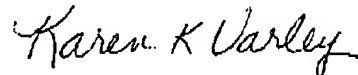
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CONCLUSION

Please charge applicable fees to Deposit Account No. 16-1852 as shown on the enclosed Fee Transmittal.

Applicants believe that all claims under consideration are in condition for allowance, and such action is respectfully requested.

Respectfully submitted,



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